CHEST Online Supplement

Pulmonary Edema Following Initiation of Parenteral Prostacyclin Therapy for Pulmonary Arterial Hypertension

A Retrospective Study

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e-Appendix 1.

Results

Four out of the 33 patients with pulmonary edema had that diagnosis based solely on new or worsening pleural effusions. Excluding those 4 subjects, the frequency of pulmonary edema was 29/155 patients (18.7%, 95% CI 13.4 – 25.6%). The tables in this supplement report study results using the revised definition of pulmonary edema i.e. reclassifying the 4 subjects in whom pulmonary edema was diagnosed based solely on new or worsening pleural effusion. Results did not change significantly. Baseline differences were largely the same, with the exception of a lower proportion of males and higher mPAP in the pulmonary edema group (e-Table 1). Elevated RAP, 3 or more risk factors for LHD, and CTD-PAH remained independent predictors of pulmonary edema, the latter with a weaker association. In addition, male sex had a borderline association with a lower risk of developing pulmonary edema (e-Table 2). Pulmonary edema was associated with a mean increase of 4.45 days in hospital LOS (95% CI 1.44 – 7.47, p = 0.005). Pulmonary edema was associated with increased 6-month mortality (OR 3.54, 95% CI 1.04 – 12.1, p = 0.04) (e-Table 3).

e-Table 1. Baseline characteristics and comparison of patients by development of pulmonary edema.

	Overall (n=155)	No pulmonary edema (n=126)	Pulmonary edema (n=29)	p-value
Age, years	51 (39-57)	50 (39-56)	54 (43-65)	0.146
Male gender	28 (18.1%)	27 (21.4%)	1 (3.4%)	0.045
Caucasian	132 (85.2%)	107 (84.9%)	25 (86.2%)	1
BMI Kg/m2	27 (23-33)	27 (22-32)	29 (25-33)	0.351
PH subtype				0.115
IPAH	99 (63.9%)	84 (66.7%)	15 (51.7)	
CTD-PAH	36 (23.2%)	25 (19.8%)	11 (37.9%)	
Other	20 (12.9%)	17 (13.5%)	3 (10.3%)	
DM prevalence %	23 (15.4%)	17 (13.5%)	6 (20.7%)	0.488
CAD prevalence %	13 (8.3%)	9 (7.1%)	4 (13.8%)	0.428
HTN prevalence %	62 (41.9%)	48 (38.1%)	14 (48.3%)	0.424
Atrial fibrillation	8 (5.2%)	7 (5.6%)	1 (3.4%)	1
FVC percentage %	79 (66-89)	80 (68-89) n=104	74 (62-79) n=21	0.087
DLCO percentage %	58 (41-73)	62 (42-74) n=93	48 (35-64) n=19	0.08
DLCO <55%	49 (43.7%) n=112	36 (38.7%) n = 93	13 (68.4%) n = 19	0.02
LV ejection fraction %	55 (55-60)	55 (55-60)	55 (55-60)	0.114
LV diastolic dysfunction	77 (50.7%)	64 (52%)	13 (44.8%)	0.623
RAP, mmHg	12 (7-17)	11 (7-16)	18 (8-20)	0.006
mPAP, mmHg	55 (47-63)	55 (46-61)	61 (50-70)	0.035
PAWP, mmHg	11 (8-16)	10 (8-15)	13 (9-17)	0.072
CI, L/min/m2	1.9 (1.6-2.4)	1.91 (1.6-2.4)	1.70 (1.5-2.1)	0.123
PVR, Wood units	12 (8-16)	11 (8-15)	13 (9-18)	0.104
LA diameter cm	3.61 (0.67)	3.62 (+0.66)	3.57 (+0.76)	0.748
LA size percentage				0.131
Normal	127 (84.7%)	102 (84.3)	25 (86.2)	
Mild	16 (10.7%)	13 (10.7)	3 (10.3)	
Mod	6 (4.0%)	6 (5.0)	0 (0.0)	
Severe	1 (0.7%)	0 (0.0)	1 (3.4)	
LHD risk factors $\geq$ 3 (%)	12 (7.7%)	6 (4.8)	6 (20.7)	0.012

BMI = body mass index; CAD = coronary artery disease; CI = cardiac index; CTD-PAH = connective tissue disease-associated pulmonary arterial hypertension; DLCO = diffusion capacity of lung for carbon monoxide; DM = diabetes mellitus; FVC = forced vital capacity; HTN = hypertension; IPAH = idiopathic pulmonary arterial hypertension; LA: = left atrium; LHD = left heart disease; mPAP = mean pulmonary artery pressure; PAWP = pulmonary artery wedge pressure; PH = pulmonary hypertension; PVR = pulmonary vascular resistance; RAP = right atrial pressure.
Data are presented as count (%) and median (25th – 75th percentile).

e-Table 2. Predictors of pulmonary edema in a multivariable logistic regression model.

	Odds Ratio	95% CI	p-value
Age	1.02		ns
Male gender	0.12		0.06
Caucasian	2.02		ns
CTD-PAH vs. IPAH	3.08	0.84-11.23	0.08
FVC percentage	0.99		ns
DLCO percentage	0.99		ns
LVEF	1.03		ns
LV diastolic dysfunction	0.49		ns
RAP*	2.87	1.13-7.24	0.02
mPAP	1.0		ns
PAWP	1.07		ns
CI	3.54		ns
PVR	1.24		ns
LHD risk factors ≥3	5.99	1.29-27.82	0.02

CI = cardiac index; CTD-PAH = connective tissue disease-associated pulmonary arterial hypertension; DLCO = diffusion capacity of lung for carbon monoxide; FVC = forced vital capacity; IPAH = idiopathic pulmonary arterial hypertension; LHD = left heart disease; LVEF = left ventricular ejection fraction; mPAP = mean pulmonary artery pressure; PAWP = pulmonary artery wedge pressure; PVR = pulmonary vascular resistance; OR = odds ratio;   RAP = right atrial pressure. * Odds ratio is for the comparison of RAP of 17 versus 7 mmHg.

e-Table 3. Survival at discharge, 1, 3 and 6 months by development of pulmonary edema.

	Overall (n=155)	No pulmonary edema (n=126)	Pulmonary edema (n=29)	p-value
Alive at discharge	154 (99.4%)	126 (100%)	28 (96.6%)	0.42
PGI2 dose at discharge				
Epoprostenol	6 (5-8)	6 (5-8)	7.5 (5-9)	0.24
Treprostinil	15 (9-18.5)	16.5 (11-18.5)	9 (7.5-21)	0.32
Alive 1 month	152 (98.1%)	126 (100%)	26 (89.7%)	0.004
Alive 3 months	150 (96.8%)	125 (99.2%)	25 (86.2%)	0.003
Alive 6 months	143 (92.3%)	119 (94.4%)	24 (82.8%)	0.082
ICU LOS	3 (2-4)	3 (2-4)	3 (2-5)	0.283
Hospital LOS	6 (4-8)	5 (4-8)	8 (5-14)	0.003

ICU = intensive care unit; LOS = length of stay; PGI2 = prostacyclin analogue.

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